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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/817,622	GARLICH ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/15/04; 10/18/04; 4/2/04; and 3/17/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *3-5,8-10,15,16,21,22,24,26,28,30,32,34 and 38-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,11-14,17-20,23,25,27,29,31,33,35-37 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/04; 10/18/04; & 4/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

APPLICANT'S INVENTION

1. Applicant's invention is directed to methods comprising compositions comprising a cell protection factor, linked to a bone targeting agent.

Note: Claims 1-75 are pending.

RESPONSE TO APPLICANT'S ELECTION

2. Applicant's election with traverse of Group III (claims 1, 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 31, 33, 35-37, and newly added claim 75 filed 3/17/06. The traversal is on the grounds that the available evidence does not justify the restriction requirement and it is likely that the search results would overlap significantly. This is found non-persuasive because the formulae of the cell protection factors encompassed by the instant invention are structurally different. Thus, a separate search of the art is necessary for each formula. Also, since the formulae are structurally different prior art which anticipates or renders obvious one group would neither anticipate nor render another group obvious. For example, Formula I disclose a =NH group attached to the five membered sulfur and nitrogen containing ring while Compounds of Formula IV disclose a five membered ring containing a nitrogen group and a second nitrogen atom that overlaps with that of the five membered ring containing a sulfur and nitrogen group. Thus, the products are materially different in structure and element . Also, it is noted that the restriction was also performed on the basis that the process for using the product as set forth in the instant invention may be practice with a materially different product (for example, the method of inhibiting cell death may be performed using

multiple products, the products of the various Formulae). Hence, the restriction requirement is still deemed proper and is therefore made FINAL.

The Examiner also acknowledges Applicant's election of the species pifithrin-β shown in Figure 2. The search was not extended beyond Applicant's elected species because prior art was found which could be used to reject Applicant's claims.

WITHDRAWN CLAIMS

3. Claims 3-5, 8-10, 15, 16, 21, 22, 24, 26, 28, 30, 32, 34, and 38-74 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

112 FIRST PARAGRAPH REJECTIONS

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 31, and 33, 35-37, and 75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *cell protection factors* selected from compounds of Formulae I-X, does not reasonably provide enablement for all cell protection factors which are capable of being linked to a bone targeting agent. Also, while Applicant is enabled for *bone targeting agent* selected from the group consisting of phosphonates, aminophosphonates, bisphosphonates, hydroxydiphosphates, and acidic polypeptides, the disclosure does

not reasonably provide enablement for all bone targeting agents. Furthermore, while Applicant is enable for the enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical *linkers*, the disclosure does not reasonably provide enablement for all cleavable linkers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed a method of inhibiting cell death in a mammal wherein a subject is administered a composition comprising a cell protection factor covalently linked to a bone targeting agent via a cleavable linker.

(2) State of the prior art

The references do not indicate which all possible cell protection factors, bone targeting agents, and linkers which are useful with the claimed invention.

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. Independent claim 1 encompasses a vast number of possible cell protection factors, bone targeting agents, and linker combinations. Applicant's specification does not enable the public to make or use such a vast number of possible compositions.

(4) Level of predictability in the art

The art pertaining to the inhibiting cell death is highly unpredictable. Determining the various types of cell protection factor, linker, and bone targeting agent combinations that will be applicable to all method of inhibiting cell death requires various experimental procedures and without guidance that is applicable to all mammals would result in little predictability in performing the claimed invention, absent some guidance.

(5) Amount of direction and guidance provided by the inventor

Independent claim 1 encompasses a vast number of compositions. Applicant's limited guidance does not enable the public to prepare such a numerous amount of cell protection factor, linker and bone targeting agent combinations. There is no directional guidance for the particular, cell protection factors, bone targeting agent, or linkers other that those specifically set forth above. Hence, there is no enablement for all possible permutations and combinations of the compositions comprising a bone targeting agent, a cell protection factor, and linker.

(6) Existence of working examples

Independent claim 1 encompasses a vast number of compositions. Applicant's limited working examples do not enable the public to prepare such a numerous amount

of the bone targeting agent, a cell protection factor, and linker composition. While Applicant's claims encompass a plethora of possible bone targeting agents, cell protection factors, and linkers, the specification provides limited combinations of the composition.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible bone targeting agents, a cell protection factors, and linkers known to exist.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. Furthermore, based on the unpredictable nature of the invention, the state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

112 SECOND PARAGRAPH REJECTION

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 31, and 33, 35-37, and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 31, and 33, 35-37, and 75: The claims as written are ambiguous because in independent claim 1, it is unclear what conditions Applicant's is referring to by the phrase 'linkage is cleaved under physiological condition' . Thus, since dependent claims 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 31, and 33, 35-37, and 75 depend on independent claim 1, those claims are also vague and indefinite.

103 REJECTION

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 6, 7, 11-14, 17-20, 23, 25, 27, 29, 35-37, and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gudkov et al (US Patent No. 6,593,353).

Gudkov et al disclose p53 inhibitors and uses thereof in the treatment of p-53 mediated diseases, conditions, and injuries (see entire documents, especially, abstract). In addition, Gudkov et al disclose (1) that one role of p53 is to act as a tumor suppressor by mediating apoptosis and growth arrest in response to a variety of stresses and controlling cellular senescence (column 2, lines 62-65; column 5, lines 12-

16). (2) Temporary p53 inhibitors are effective in reducing or eliminating p53 dependent neuronal death in the central nervous system; the preservation of tissues and organs prior to transplanting; preparing a host for bone marrow transplantation; and reducing or eliminating neuronal damage during seizures (column 3, lines 13-19). (3) Gudkov et al disclose a Formula III (column 4, line 40; column 9, lines 20-29 and 40 and 45) that encompasses Applicant's elected species when X = sulfur, R1 and R2 taken together form a six-membered ring, R3 is a aryl group (i.e., phenyl) substituted with an alkyl group (i.e., methyl group). The specific elected species is disclosed in column 15, line 27 and column 17, line 15. (4) In order to improve cancer treatment, the composition comprises a chemotherapeutic drug and a temporary p53 inhibitor (column 5, lines 29-32). (5) Also, the composition may comprising a drug capable of treating a p53 related disease and a temporary p53 inhibitor or a temporary p53 inhibitory and a carrier (column 5, lines 33-64). The compounds of Formula III which contain acidic moieties can form pharmaceutically acceptable salts with suitable cations. The pharmaceutically acceptable salts of the compounds which contain a basic center are acid addition salts formed with pharmaceutically acceptable acids such as phosphate, hydrogen phosphate, etc. (column 11, lines 23-36). While Gudkov et al does not disclose a specific example wherein the cell protection factor is covalently linked to a bone targeting agent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to generate a method of inhibiting cell death in a mammal by administering a composition comprising a cell protection factor covalently linked to a bone targeting agent because Gudkov et al, like Applicant, disclose a temporary p53

inhibitor, pifithrin-β, capable of inhibiting cell death optionally, in combination with a carrier, chemotherapeutic agent, drug, etc. Thus, a skilled practitioner in the art would recognize that since the compositions of Gudkov et al a capable of targeting tumors, bone marrow components, etc., a bone targeting agent would be obvious. Furthermore, since independent claim 1 does not set forth the particular type of linkage(s) Applicant is/are referring to then a skilled artisan would recognize that some type of linkage occurs in the composition between the cell protection factor and the bone targeting agent.

CLAIM OBJECTIONS

10. Claims 31 and 33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. L. Jones
Primary Examiner
Art Unit 1618

September 29, 2006